PATENT
Attorney Docket No.: 47259-5001-00-US (223490)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Confirmation No.: 9193
Kazuaki OKUNO et al.	)	
Application No.: 10/573,821	)	Group Art Unit: 1652
Filed: March 28, 2006	)	Examiner: Sheridan L. Swope

For: POLYPEPTIDE CLEAVAGE METHOD USING OmpT PROTEASE VARIANT

PETITION UNDER 37 C.F.R. § 1.144

Mail Stop: AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandra, Virginia 22313-1450

Sir:

The present petition is filed in response to the non-final Office Action mailed May 14, 2009, in the application above. This Petition is timely filed on or before September 14, 2009, because of the concurrently filed petition for a ONE month extension of time. This Petition is properly filed under 37 C.F.R. § 1.144, because the Office alleges a lack of unity of invention. No appeal has been filed yet in this application. *See* 37 C.F.R. § 1.144.

Statement of Facts begins on page 2.

Points to be Reviewed begin on page 4.

Actions Requested begin on page 8.

STATEMENT OF FACTS

FF.1 On 22 May 2008, the Office issued a Requirement for Restriction/Election in the present application.

FF.2 On 21 November 2008, Petitioners filed a Response to Restriction Requirement.

FF.3 On 7 January 2009, the Office issued a Notice of Non-Responsive Amendment.

FF.4 On 16 January 2009, following an interview with Petitioner's counsel, the Office withdrew the Required issued 22 May 2008 and issued a Revised (Second) Requirement for Restriction/Election.

FF.5 On 9 February 2009, following an interview with Petitioner's counsel and Examiner J. Burke, USPTO Quality Assurance Specialist, the Office withdrew the two previous Requirements for Restriction/Election and vacated the Notice of Non-Responsive Amendment. In their place, the Office issued a Revised (Third) Requirement for Restriction/Election.

FF.6 In the 9 February 2009 Office Action, the Examiner required an election of a single species from each of Group (A) and Group (B):

(A) An OmpT protease 97th amino acid variant, where the species has one of the specific amino acid residues at the 97th position recited in claim 12-17, for example; and

(B) A cleavage motif from the group consisting of the motifs described in claims 1-9, 11-14, and 26-35.

FF.7 An OmpT protease 97th amino acid variant differs from a wild type OmpT sequence by one amino acid substitution at the 97th amino acid residue. *See, e.g.*, Specification, p. 27, last paragraph.

FF.8 The Office alleged that "Okuna et al., 2002 (IDS) . . . anticipates Claim 1." Office Action issued 9 February 2009, p. 4, lines 9-10.

FF.9 Petitioners believe the Office referred to Okuno et al., "Substrate Specificity at the P1' Site of *Escherichia coli* OmpT under Denaturing Conditions," *Biosci. Biotechnol. Biochem.* 66: 127-134 (2002).

FF.10 The Office independently alleged:

> Furthermore, the proteases of species (A) do not share a common structure and function, as defined by cleavage specificity (Table 1 & Fig. 3). Office Action, p. 4, lines 12-13.

FF.11 The Office further alleged:

> Likewise, the species (B) . . . do not share a common structure and function, as defined by the ability to be cleaved by any encompassed protease (Table 1 & Fig. 3). *Id.*, lines 10-12.

FF.12 On 3 April 2009, Petitioners filed a Response to Third Restriction Requirement. The listing of claims presented in this response replaces all other listing of claims in this application.

FF.13 For Group (A), Petitioners elected the embodiment where the 97th amino acid is Met, *i.e.*, methionine (claim 13).

FF.14 For Group (B), Petitioners elected the embodiment where the cleavage motif is SEQ ID NO: 12 (claim 11).

FF.15 Petitioners elected WITH TRAVERSE.

FF.16 Petitioners provided detailed reasons why Okuno et al., "Substrate Specificity at the P1' Site of *Escherichia coli* OmpT under Denaturing Conditions," *Biosci. Biotechnol. Biochem.* 66: 127-134 (2002) does not anticipate the claims.

FF.17 On 14 May 2009, the Office acknowledged that the election of species was responsive and made the restriction requirement FINAL.

FF.18 While the 14 May 2009 Office Action responded to Petitioners' arguments that Okuna does not anticipate the claims, the Examiner did not use Okuna in an art rejection.

FF.19 The Examiner maintained the allegation that Groups (A) and (B) are directed to improper Markush groups. The Examiner alleged that unity of invention is determined with respect to the invention as a whole and that "a subset of claims cannot have unity of invention." *See* Office Action, p. 3, lines 7-9.

FF.20 The present application is a National Stage application, so the rules and procedures governing restriction requirements must conform to the Patent Cooperation Treaty (PCT). *See* PCT Article 27.

POINTS TO BE REVIEWED

1. The Examiner must withdraw the objection to unity of invention or apply Okuna in a rejection under 35 U.S.C. § 102.

The Examiner alleges the claims lack unity of invention because of alleged anticipation by "Okuna 2002." *See* FF.8. Okuna does not anticipate the claims for the reasons set forth at length in Petitioners' Response to Third Restriction Requirement filed April 3, 2009, and in the Response filed concurrently with the present petition.

Irrespective of whether Okuna anticipates Claim 1, however, the Examiner has not rejected any claim in this application under 35 U.S.C. § 102 as anticipated by Okuna. *See* FF.18. 35 U.S.C. § 372(a), "National stage: Requirements and procedure," provides (emphasis added):

> ***All questions of substance*** and, within the scope of the requirements of the treaty and Regulations, procedure in an international application designating the United States shall be determined as in the case of national applications regularly filed in the Patent and Trademark Office.

Whether a prior art reference anticipates any claim of an application is unquestionably a "question of substance" under 35 U.S.C. § 372. Section 372 requires the Office to determine the merits of alleged anticipation by Okuna in this National Stage application, as it would in any national application regularly filed in the Patent and Trademark Office. Further, MPEP § 1893.03(d) requires the Examiner to determine the merits of the elected species *inter alia* under 35 U.S.C. § 102—not in the context of PCT rules relating to unity of invention—before rejoinder can be considered:

> If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder.

Finally, using Okuna in a rejection would clarify that the Board of Patent Appeals and Interferences has subject matter jurisdiction to review alleged anticipation by Okuna.[1]

Accordingly, Petitioners request the Office to remand the application to the Examiner for reconsideration of Petitioners' arguments, with the instruction either to withdraw the allegation that "Okuna 2002 . . . anticipates Claim 1," or to state grounds for a rejection under 35 U.S.C. § 102.

2. Group (A), directed to OmpT protease 97th amino acid variants recited in claim 12, is a proper Markush group that possesses unity of invention under PCT Rule 13.2.

The Office independently alleges that Group (A) represents an improper Markush group and thus lacks unity of invention. *See* FF.10, 19. Claim 12 is a generic claim directed to a process of using an OmpT protease 97th amino acid variant, wherein the 97th amino acid from the N-terminus of the OmpT protease is alanine, leucine, phenylalanine, methionine, serine, threonine, cysteine, asparagine, glutamine, glutamic acid, or histidine.

MPEP § 1850 states that Markush groups directed to alternatives of chemical compounds have unity of invention when the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

Group (A) has unity of invention, under this test. Claim 12 satisfies prong (A) of the test above, because the OmpT protease 97th amino acid variants have a "common property or activity." Namely all are proteases capable of cleaving a protease recognition site. *See, e.g.*, Specification, p. 1, lines 5-23.

Claim 12 complies with the (B)(1) prong, because the variants share a "significant structural element." Each OmpT protease 97th amino acid variant, for example, is structurally

[1] The BPAI has subject matter jurisdiction to review alleged anticipation by Okuna in the absence of an explicit rejection. *Cf. In re Haas*, 179 USPQ 623, 625-26 (CCPA 1973) (holding that the Board of Patent Appeals and

the same as its wild type counterpart, except for one amino acid substitution. *See* Specification, p. 27, last paragraph. Although the Examiner alleges lack of unity because the "proteases of species (A) do not share a common structure ***and*** function" (FF.10, emphasis added), the PCT test is disjunctive. That is, unity of invention is found, when the claim complies with ***either*** the (B)(1) ***or*** (B)(2) prong.[2] In this case, the claim has unity of invention, because it complies with at least the (B)(1) prong.

Further, claim 12 satisfies the (B)(2) prong. In this context, the Examiner cites Table 1 (*see* FF.10), which shows that OmpT protease 97th amino acid variants have different levels of activity against the different the substrates shown in FIG. 1. *See, e.g.*, Specification, Table 1, and p. 44, line 27. The Examiner apparently alleges that claim 12 hence does not meet the (B)(2) prong of the test above. However, Petitioners have met the (B)(1) prong, so the assertion regarding (B)(2) is moot.

Table 1 shows that each of the recited variants has protease activity. The variants are members of a recognized class of compounds, because each variant can be substituted for another and still achieve the same intended result—the ***claimed*** result—of cleaving a peptide recognition site. That is all that is needed to comply with the (B)(2) prong. The Examiner assumes that each protease must have the same specificity toward the same substrate (*see* FF.10), but the claim ***as a whole*** does not define the OmpT protease 97th amino acid variant on the basis of specificity toward any particular substrate sequence. In essence, the Examiner improperly imports limitations from the specification into the claims. For this reason, claim 12 complies with the (B)(2) prong of the test above.

The Examiner further argues that "a subset of claims cannot have unity of invention." *See* FF.19. This allegation has no basis in PCT rules, nor does the Examiner state such a basis. PCT Rule 13.2, in fact, expressly permits unity of invention on the basis of a plurality of special technical features. In the present case, the claims are united by the special technical feature of the cleavage site recited in claim 1 and the special technical feature of the OmpT protease 97th amino acid variant recited in claim 12.

Interferences has subject matter jurisdiction over a refusal to rejoin non-elected species, following an indication that the elected species is allowable).

For all the reasons above, the species of Group (A) possess unity of invention. *See* MPEP § 1850. Accordingly, Petitioners request the Office to indicate that Group (A) is a proper Markush group.

3. Group (B), directed to OmpT protease cleavage motifs recited in claim 1, is a proper Markush group that possesses unity of invention under PCT Rule 13.2.

The Examiner alleges that Group (B) represents an improper Markush group and thus lacks unity of invention. Claim 1 is a generic claim. As presently amended, claim 1 is directed to a process of using a polypeptide comprising arginine or lysine at the P1 position of a desired cleavage site, an amino acid other than aspartic acid, glutamic acid or proline at the P1' position, and a single basic amino acid or two or three consecutive basic amino acids situated at any site in the amino acid sequence from the P10 position to the P3 position or from the P3' position to the P5' position, wherein, if there is only a single basic amino acid situated in the amino acid sequence from the P10 position to the P3 position, the single basic amino acid is situated at a position other than the P6 or the P4 position.

Group (B) has unity of invention, under this test above. First, claim 1 satisfies prong (A), because all the recited cleavage motifs have the common property of conferring enhanced OmpT protease cleavage efficiency at P1-P1'.

Second, claim 1 complies with the (B)(1) prong, because the variants share a "significant structural element." Taking claim 1 as a whole, each cleavage site shares the structural element of a polypeptide comprising:

> arginine or lysine at the P1 position of a desired cleavage site, an amino acid other than aspartic acid, glutamic acid or proline at the P1' position, and a single basic amino acid or two or three consecutive basic amino acids situated at any site in the amino acid sequence from the P10 position to the P3 position or from the P3' position to the P5' position, wherein, if there is only a single basic amino acid situated in the amino acid sequence from the P10 position to the P3 position, the single basic amino acid is situated at a position other than the P6 or the P4 position.

---

[2] *See also* J. Burke, USPTO, "Unity of Invention Biotechnology Practice," *at* http://www.uspto.gov/web/patents/biochempharm/documents/burke.pps (last updated September 29, 2006).

Certainly, many possible sequences are encompassed by claim 1. Each encompassed sequence, however, shares a combination of structural features common to all the claimed recognition sites and important to the function of the cleavage sites within the claim as a whole. That is enough to satisfy the (B)(1) prong of the test above.

Finally, claim 1 also satisfies the (B)(2) prong, because each species of OmpT protease cleavage site in claim 1 can be cleaved by an OmpT protease. As in Part 2 above, the cleavage sites are members of a recognized class of compounds, because each cleavage site can be substituted for another and still achieve the same intended result—the ***claimed*** result—of being cleaved by an OmpT protease. That is all that is needed to comply with the (B)(2) prong.

For all the reasons above, the species of Group (B) possess unity of invention. *See* MPEP § 1850. Accordingly, Petitioners request the Office to indicate that Group (B) is a proper Markush group.

4. The Examiner has no authority to object to claims 12, 15-16, 23, and 26-27 for reciting non-elected subject matter, and the objection accordingly should be withdrawn.

The Examiner objects to claims 12, 15-16, 23, and 26-27 for reciting non-elected subject matter. There are no provisions under the PCT, Title 35 of the patent statutes, Title 37 of the Code of Federal Regulations, or the MPEP that authorize an objection to a claim for reciting non-elected species. Petitioners thus request the Office to instruct the Examiner to withdraw the objection.

ACTIONS REQUESTED

(1) Petitioners request the Office to remand the application to the Examiner for reconsideration of Petitioners' arguments, with the instruction either to withdraw the allegation that "Okuna 2002 . . . anticipates Claim 1," or to state grounds for a rejection under 35 U.S.C. § 102. *See* Part 1 above.

(2) Petitioners request the Office to indicate that claim 12 of Group (A) is a proper Markush group, within the PCT rules. *See* Part 2, above.

(3) Petitioners request the Office to indicate that claim 1 of Group (B) is a proper Markush group, within the PCT rules. *See* Part 3, above.

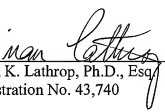
(4) Petitioners request the Office to withdraw the objection of claims 12, 15-16, 23, and 26-27 for reciting non-elected subject matter. *See* Part 4, above.

CONCLUSION

Should the Office have any questions regarding this Petition, please contact Petitioners' undersigned representative at (202) 842-8862. Please direct all correspondence to the below-listed address.

If the Office believes fees are due in the above-referenced matter, or if fees are due to maintain pendency of this application, the Office is authorized to charge the outstanding fees to Deposit Account No. 50-0573. The Office is likewise authorized to credit any overpayment to the same Deposit Account Number.

Respectfully Submitted,

Date: September 14, 2009 By: 

Brian K. Lathrop, Ph.D., Esq.
Registration No. 43,740

DRINKER BIDDLE & REATH LLP
Customer No. **55694**
1500 K Street, N.W., Suite 1100
Washington, D.C. 20005-1209
Tel. No.: (202) 842-8800
Fax No.: (202) 842-8465